LETTERS TO THE EDITORS

The Editors invite readers to submit letters commenting on the contents of articles that appear in the JOURNAL. Also welcome are brief communications in letter form reporting investigative or clinical observations without extensive documentation and with brief bibliography (five titles or less), not requiring peer review but open to critique by readers. Letters to the Editors should be no more than 500 words in length and they may have to be edited for publication.

Regarding "What you didn't know about the NASCET"

To the Editors:

As a member of the Data Monitoring Committee of the North American Symptomatic Carotid Endarterectomy Trial (NASCET), as mentioned by Dr. D. Eugene Strandness in his commentary (J VASC SURG 1995;25:163-5), I feel constrained to offer my own comments in the light of the references to my role in the committee.

I was keenly aware of the reports of a number of my vascular surgery colleagues, whose opinions I respected and whose conclusions confirmed those that I had reached based on my own experience—namely, that severe carotid artery stenosis corrected by surgical intervention with a sufficiently low operative complication rate results in relative protection from future stroke. So, armed with a background of experience with randomized clinical trials and sustained by personal experience with more than 1500 surgical patients, I accepted the invitation to join the data monitoring committee of NASCET. Although I had personal reservations about contributing patients, I felt that I might lend credibility to the outcome of the study, whatever it might be.

There appeared to be an adversarial relationship between the principal investigator and the data monitoring committee. When the difficult and pointed questions that need to be asked during any clinical trial were asked, they were often met with a defensive posture by the principal investigator. This impression appears to be confirmed by the correspondence that Dr. Barnett had with Dr. Michael Walker, cited by Dr. Strandness. To the credit of Dr. Walker and the NIH group, when I asked for an emergency meeting when the favorable results of surgical intervention for severe carotid stenoses became apparent, to consider the question of what was to be done with patients who were entered into the middle moderate stenosis group and who had proceeded to preocclusive stenosis, the meeting was held.

For the data monitoring committee to be effective and contribute to the acceptance of the results, very pointed questions must be raised during its deliberations. Such questions now almost inevitably introduce adversarial positions and animosities. In essence, how to organize prospective, randomized clinical trials needs to be reevaluated so that they cease to be vehicles for career advancement and so that repetition and reduplication become unnecessary, because it is our patients who suffer in these trials. Not only do they suffer because of the need to weigh conflicting evidence presented by physicians who have vested interests in the outcome of the trials and who must adopt dual, often conflicting, roles—compassionate physician versus dispassionate, coldly objective investigator—but also because they may surrender their rights to meaningful treatment. It does no good to invoke the greater good that will result from the studies if a trial turns out to be inconclusive because of procedural problems, conceptual deficiencies, or personality conflicts. Shouldn't the recruitment of the patients be performed by nonparticipants of the studies who have no vested interest in the outcome? These are issues that are at the heart of the comments offered by Dr. Strandness, issues that could jeopardize the acceptance of any large clinical trial. I agree with Dr. Strandness that the data monitoring committee should be privy to the data in an ongoing fashion, but as long as the investigators feel that they are the "owners" of the trial and of the data, and as long as the protocols are flawed from the start, how can a data monitoring committee be as effective as it might?

The NASCET has made a great contribution in preventing strokes, albeit with a higher than desirable or achievable surgical complication rate,[1] by helping to validate the voluminous evidence regarding the efficacy of carotid endarterectomy for advanced carotid disease detected by measuring the degree of carotid stenosis with angiography. It still leaves us with the fundamental and much debated questions, "What is the validity of measuring carotid stenosis on an angiogram, by whatever technique, as the sole criterion for undertaking carotid endarterectomy? How should it be measured?[2,3] Wouldn't the flow/velocity studies emphasized by Gene Strandness have helped to at least clarify quantification of stenosis when combined with angiography?" The futility of attempting to differentiate between 79% stenoses and 81% stenoses is obvious, if by no other data than the inability to precisely equate stenoses measured in the European Carotid Endarterectomy Trial[4] and NASCET, whose clinical outcomes were nevertheless identical. It was realized before either trial was begun that the critical factor of carotid plaques in causing strokes was plaque composition. Yet both studies failed to deal with these data.

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REFERENCES

1. Report of the Committee on Health Care Issues. ANA. Does carotid endarterectomy decrease the risk of stroke and death in patients with transient ischemic attacks? Ann Neurol 1978;22: 72-6.
2. Rothwell PM, Gibson RJ, Slattery J, et al. Equivalence of measurement of carotid stenosis: a comparison of three methods on 1001 angiograms. Stroke 1994;25:2445-9.
3. Eliasziw M, Smith RF, Singh N, et al. Further comments on measurement of carotid stenosis from angiograms. Stroke 1994;25:2445-9.
4. European Carotid Surgery Trialists Collaborative Group. MRC. European carotid surgery trial: interim results for symptomatic patients with severe (70-99%) or mild (0-29%) carotid stenosis. Lancet 1991;337:1235-7.

Regarding "What you didn't know about the NASCET"

To the Editors:

In a recent editorial (J VASC SURG 1995;25:163-5), Dr. Eugene Strandness raised several concerns about the data monitoring committee of the North American Symptomatic Carotid Endarterectomy Trial (NASCET). Because of the importance of the trial and the seriousness of the concerns, I asked a group of four consultants (one from the National Heart, Lung, and Blood Institute and three from outside of the National Institutes of Health) to meet and review the procedures used by the National Institute of Neurological Disorders and Stroke (NINDS) in organizing and guiding the monitoring committee for NASCET. The consultants looked specifically at the question of whether the results of the trial were jeopardized because of the issues raised by Dr. Strandness, and found that they were not. They also found no evidence of misconduct by the NINDS staff. The consultants emphasized, however, that several aspects of the way that the data monitoring committee for NASCET has been operated could be improved, and suggested that NINDS review the procedures by which we organize and guide data- and safety-monitoring committees. As a result, NINDS is now formulating a new set of guidelines for these procedures. These guidelines will be made available to the research community when they are completed. We are grateful to Dr. Strandness for raising these issues and hope that we will be able to serve the clinical research community even more effectively as a result of these changes.

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Editors' Comments

These two letters conclude what has been perceived as a very vexing problem that faces investigators participating in clinical research initiatives that involve patients with vascular diseases. The Editors particularly appreciate Dr. Hall's response, which notes that NINDS is "formulating a new set of guidelines" to address the concerns that Dr. Strandness expressed in his special communication in the January 1995 issue of the Journal of Vascular Surgery.

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Editors